Repetitive electrostatic pressurised intraperitoneal aerosol chemotherapy with oxaliplatin as a palliative monotherapy for isolated unresectable colorectal peritoneal metastases: protocol of a multicentre, open-label, single-arm, phase II study (CRC-PIPAC)

Published: 12-06-2017
Last updated: 13-04-2024

To prospectively explore the feasibility safety, tolerability, preliminary efficacy, costs, and pharmacokinetic profile of repetitive ePIPAC-OX as a palliative monotherapy for isolated unresectable colorectal PM under controlled circumstances.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON49271

Source
ToetsingOnline

Brief title
CRC-PIPAC

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Metastases
- Gastrointestinal therapeutic procedures

Synonym
Unresectable isolated colorectal peritoneal metastases; inoperable peritoneal metastases of large bowel cancer

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis
Source(s) of monetary or material Support: Catharina Onderzoeksfonds en St. Antonius Onderzoeksfonds

Intervention

Keyword: Colorectal Cancer, Intraperitoneal Chemotherapy, Oxaliplatin, Peritoneal Metastases

Outcome measures

Primary outcome

The number of patients with major toxicity (grade *3 according to the Common

Terminology Criteria for Adverse Events v4.0) up to four weeks after the last

procedure.

Secondary outcome

Secondary outcomes are:

* the environmental safety of ePIPAC-OX, based on air concentrations (measured

by RPS Analyse, Breda, Netherlands) and surface concentrations (measured by

Pharmacy, Cathari-na Hospital, Eindhoven, Netherlands) of oxaliplatin during

the first three procedures, measured by atomic absorption spectrophotometry;

* procedure-related characteristics of ePIPAC-OX (e.g. laparoscopic access,

intraoperative complications, amount of adhesions, technical difficulties,

operating time);

* the number of procedures in each patient and reasons for discontinuation;

* minor toxicity, defined as grade *2 according to CTCAE v4.0 [120], up to four weeks after the last ePIPAC-OX;

* organ-specific toxicity, based on bone marrow, liver, and kidney functions measured at dif-ferent time points (Table 1);

* major and minor postoperative complications, defined as grade *3 and grade *2 according to Clavien-Dindo [121], respectively, up to four weeks after the last ePIPAC-OX;

* hospital stay, defined as the number of days between ePIPAC-OX and initial discharge;

* readmissions, defined as any hospital admission after initial discharge, up to four weeks af-ter the last ePIPAC-OX;

* radiological tumour response, based on central review of thoracoabdominal CT and DW-MRI at baseline and four weeks after each ePIPAC-OX, performed by two independent ra-diologists (JN, MLH) blinded to clinical outcomes (classification is not defined a priori);

* histopathological tumour response, based on central review of collected peritoneal biop-sies during each ePIPAC-OX, performed by two independent pathologists (e.g. CJRH) blind-ed to clinical outcomes by using the Peritoneal Regression Grading Score [122];

* cytological tumour response, based on collected ascites or peritoneal washing cytology dur-ing each ePIPAC-OX;

* macroscopic tumour response, based on PCI and ascites volume during each ePIPAC-OX;

* biochemical tumour response, based on tumour markers measured at different

time points (Table 1);

* quality of life, extracted from questionnaires (EQ-5D-5L, QLQ-C30, QLQ-CR29)

at different time points (Table 1);

* costs, derived from the Dutch costing guidelines for health care research at

the time of analysis, based on case report forms, hospital information systems,

and questionnaires (iMTA PCQ, iMTA MCQ) at different time points (Table 1);

* progression-free survival, defined as the time between enrolment and

clinical, radiological, or macroscopic progression, or death;

* overall survival, defined as the time between enrolment and death.

Study description

Background summary

Repetitive electrostatic pressurised intraperitoneal aerosol chemotherapy with oxaliplatin (ePIPAC-OX) is offered as a palliative treatment option for patients with isolated unresectable colorectal peritoneal metastases (PM) in several centres worldwide. As a palliative monotherapy, repetitive ePIPAC-OX may lead to intraperitoneal disease stabilisation with minimal treatment burden and preservation of quality of life. However, hardly anything is known about its feasibility, safety, tolerability, efficacy, costs, and pharmacokinetics in this setting.

Study objective

To prospectively explore the feasibility safety, tolerability, preliminary efficacy, costs, and pharmacokinetic profile of repetitive ePIPAC-OX as a palliative monotherapy for isolated unresectable colorectal PM under controlled circumstances.

Study design

Multicentre, open-label, single-arm, phase II study.

Intervention

Instead of standard palliative treatment, enrolled patients receive laparoscopy-controlled ePIPAC-OX (92 mg/m2 body-surface area [BSA]) with intravenous leucovorin (20 mg/m2 BSA) and bolus 5-fluorouracil (400 mg/m2 BSA) every six weeks. Four weeks after each procedure, patients undergo clinical, radiological, and biochemical evaluation. ePIPAC-OX is repeated until clinical, radiological, or macroscopic disease progression, after which standard palliative treatment is (re)introduced.

Study burden and risks

Standard palliative (systemic) treatment seems to be less effective for isolated unresectable colorectal PM compared to isolated unresectable non-peritoneal colorectal metastases. Moreover, palliative systemic therapy is associated with toxicity. As a palliative monotherapy, repetitive ePIPAC-OX may therefore lead to intraperitoneal disease stabilisation with a low toxicity, minimal treatment burden, and preservation of quality of life. If repetitive ePIPAC-OX leads to unacceptable toxicity or progression, this is detected in a sufficiently early stage by the frequent evaluations, after which standard palliative (systemic) treatment is reintroduced. Conclusively, the investigators feel that the potential benefits of participation outweigh the potential burden and risks.

Contacts

Public
Catharina-ziekenhuis

Michelangelolaan 2
Eindhoven 5623 EJ
NL
Scientific
Catharina-ziekenhuis

Michelangelolaan 2
Eindhoven 5623 EJ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Eligible patients are adults who have:;* a World Health Organisation (WHO) performance status of *1 and life expectancy >3 months;
* histological or cytological proof of PM of a colorectal or appendiceal carcinoma;
* unresectable disease determined by abdominal computed tomography (CT) and a diagnostic laparoscopy or laparotomy;
* adequate organ functions (haemoglobin *5.0 mmol/L, neutrophils *1.5 x 109/L, platelets *100 x 109/L, serum creatinine <1.5 x ULN, creatinine clearance *30 ml/min, and liver transaminsases <5 x ULN);
* no symptoms of gastrointestinal obstruction;
* no radiological evidence of systemic metastases;
* no contraindications for oxaliplatin or 5-fluorouracil/leucovorin;
* no contraindications for a laparoscopy;
* no previous PIPAC-procedures;
* written informed consent.;Importantly, enrolment is allowed for patients with an unresected primary tumour (if asymptomatic) and for patients in various lines of palliative treatment, including patients who refuse, have not had, or do not qualify for first-line palliative systemic therapy. All potentially eligible patients are discussed in a multidisplinary team. Enrolled patients need to be informed about the potential consequences of postponing or discontinuing standard palliative treatment by a medical oncologist prior to enrolment.

Exclusion criteria

Not applicable. See inclusion criteria.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-10-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	CapnoPen; Ultravision
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	5-fluorouracil
Generic name:	5-fluorouracil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Oxaliplatin
Generic name:	Oxaliplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Rescuvolin
Generic name:	Leucovorin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	12-06-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-07-2017

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-10-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-11-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-04-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-10-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-01-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-02-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-000927-29-NL
CCMO	NL60405.100.17
Other	NTR (NTR6603), IRSCTN (ISRCTN89947480), ClinicalTrials.gov (NCT03246321)